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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/163,272	09/29/98	DINSMORE J	DNI-041

EXAMINER	
KEEB, J	
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AMY E. MANDRAGOURAS
LAHIVE AND COCKFIELD
28 STATE STRTEET
BOSTON MA 02109

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trad marks

Office Action Summary	Application No. 09/163,272	Applicant(s) DINSMORE, JONATHAN	
	Examiner Janet Kerr	Art Unit 1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 April 2001* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,10-26 and 28-47* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,10-26 and 28-47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

Response to Amendment

The amendment filed 4/23/01 has been entered.

Claims 45-47 have been added.

Claims 1-8, 10-26, and 28-47 are pending.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Objections

Claim 10 is objected to because of the following informalities: the phrase "wherein the cell are" should be changed to "wherein the cells are" for grammatical correctness. Appropriate correction is required.

Claim Rejections - 35 USC § 112

Claims 18-26, 28-37, 43, 44, and 46 are/remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the method of treating a xenogeneic subject having spinal cord damage as observed in the animal model of amyotrophic lateral sclerosis or hemi-sected animal model, does not reasonably provide enablement for treating a xenogeneic subject having spinal cord damage resulting from the claim-designated neurodegenerative disorders, spinal cord injuries, or aging. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims for the reasons of record and the reasons below.

Applicant's arguments filed 4/23/01 have been fully considered but they are not persuasive.

It is argued that the specification enables the treatment of a variety of different types of deficits that would benefit from transplantation of fetal spinal cord cells, and furthermore, applicant has demonstrated both survival and integration of transplanted fetal porcine spinal cord cells upon transplantation into a transgenic subject (see page 9 of applicant's Response). This argument is not persuasive as the claimed invention is not limited to "fetal porcine spinal cord cells" (see, e.g., claims 18, 22-26, 28-37, 43, and 44).

It is urged that the specification provides various ways by which spinal cord cells can be administered to treat the claimed disorders. Applicant refers to working examples II and III to indicate that administering the cells by engraftment to a specific location in the spinal cord resulted in reestablishment of host spinal tracts as determined by measuring supraspinal serotonergic innervation and axonal projections from the dorsal root ganglia, and further, behavioral data demonstrates the beneficial effects of the grafts at the functional anatomical level. It is further argued that the specification discloses exemplary cell compositions and methods of administering such compositions (see pages 9-10 of applicant's Response). These arguments are not persuasive. The specification teaches obtaining a population of fetal porcine spinal cord cells from a specific embryonic age, providing the cells in an implant material, and engrafting the implant at specific sites of damage (with respect to the hemi-sected model and the ALS model). There is no guidance in the specification as to where to implant the cells in other disease or aging conditions such that the cells will survive, integrate, and result in reestablishment of host spinal tracts which are damaged as a result of diseases (other than those represented in the disclosed model systems) and aging. For example, will the physiological effects of aging which initially caused spinal cord damage have the same effect on the engrafted cells? Where in the aging spinal cord does one of skill in the art implant the cells? The specification does not provide sufficient guidance for one of skill in the art to practice the invention commensurate in scope with the claims.

Claim Rejections - 35 USC § 103

Claims 1-4, 17-21, 36, 39-45, and 47 are/remain rejected under 35 U.S.C. 103(a) as being unpatentable over Giovannini *et al.* taken with Galpern *et al.* for the reasons of record and the reasons below.

Applicant's arguments filed 4/23/01 have been fully considered but they are not persuasive. It is argued that Giovanini teaches the use of spinal cord cells from a human fetus to treat chronic contusion, and that Galpern teaches the use of ventral mesencephalic tissue from pig brain for transplantation into the brain. It is argued that the references teach the use of different populations for different disease states. It is asserted that neither of the references teach the claimed invention, nor is there motivation to combine the references to arrive at the claimed invention (see pages 12-16 of applicant's Response).

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, Giovanini *et al.* was relied upon to teach that human fetal spinal cord cells can be isolated and used in a method of treating a mammalian xenogeneic subject having spinal cord damage. Galpern *et al.* was relied upon to provide motivation for substituting human fetal spinal cord cells with porcine cells as Galpern *et al.* teach the lack of availability of human fetal tissue, the difficulties of storing human fetal tissue. Moreover, the teachings of Galpern *et al.* indicate that porcine neurons can be used to reconstruct neuronal circuitries *in vivo*. Thus, one of

ordinary skill in the art would have been motivated to isolate and use an alternative source of fetal spinal cord cells to treat spinal cord diseases/injuries, and would have had a high expectation of successfully treating the subject in need thereof with porcine fetal spinal cord cells in view of the teachings of the combined references.

Claims 1, 8, 10-12, 15, 16, 18, 25, 26, 28-31, 33, and 34 are/remain rejected under 35 U.S.C. 103(a) as being unpatentable over Giovannini *et al.* taken with Galpern *et al.*, as applied to claims 1-4, 17-21, 36, 39-45, and 47, and further in view of Chappel for the reasons of record and the reasons below.

Applicant's arguments filed 4/23/01 have been fully considered but they are not persuasive. It is argued that the reference of Chappel *et al.* does not make up for the deficiencies in the primary references. It is asserted that the reference of Chappel *et al.* with the references of Giovannini *et al.* and Galpern *et al.* (see pages 17-18 of applicant's Response).

This argument is not persuasive. As set forth above, Giovanini *et al.* was relied upon to teach that human fetal spinal cord cells can be isolated and used in a method of treating a ma does not teach the use of spinal cord cells, and further, that there is no motivation to combine the reference of Chappel *et al.* mammalian xenogeneic subject having spinal cord damage. Galpern *et al.* was relied upon to provide motivation for substituting human fetal spinal cord cells with porcine cells as Galpern *et al.* teach the lack of availability of human fetal tissue, the difficulties of storing human fetal tissue. Moreover, the teachings of Galpern *et al.* indicate that porcine neurons can be used to reconstruct neuronal circuitries *in vivo*. Thus, one of ordinary skill in the art would have been motivated to isolate and use an alternative source of fetal spinal cord cells to treat spinal cord diseases/injuries, and would have had a high expectation of successfully treating the subject in need thereof with porcine fetal spinal cord cells in view of the teachings of the combined references. With regard to Chappel *et al.*, the reference was relied upon to teach that it was known in the art to alter MHC class I antigens on cells suitable for transplantation by using a combination of molecules to alter different epitopes on the same antigen for the purpose of

reducing the immunogenicity of the cell. Thus, it would have been obvious and well within the purview of one of ordinary skill in the art to modify the immunogenicity of a population of embryonic porcine spinal cord cells for use in a xenogeneic transplantation method.

Claims 1, 5-7, 13, 14, 18, 22-24, 31, 32, 35, 37, and 38 are/remain rejected under 35 U.S.C. 103(a) as being unpatentable over Giovannini *et al.* taken with Galpern *et al.*, as applied to claims 1-4, 17-21, 36, 39-45, and 47, and further in view of Fraser, Rosenbluth *et al.*, and Wang *et al.* for the reasons of record and the reasons below.

Applicant's arguments filed 4/23/01 have been fully considered but they are not persuasive. It is argued that the references of Fraser, Rosenbluth *et al.*, and Wang *et al.* do not make up for the deficiencies in the primary references. It is asserted that the references do not teach the claimed compositions or methods of use, and further, that there is no motivation to combine the references (see pages 18-20 of applicant's Response). These arguments are not persuasive. The references of Fraser, Rosenbluth *et al.*, and Wang *et al.* were relied upon to teach that administration of specific cell populations, such as oligodendrocytes, astrocytes, and neural cells were known in the art to be suitable for xenogeneic transplantation of the cells into the spinal cord. As fetal spinal cord cells have been shown in the art to be suitable for transplanting into damaged spinal cord sites, and as specific populations of fetal spinal cord cells, e.g., oligodendrocytes and astrocytes have been shown to be effective in xenotransplantation methods, it would have been well within the purview of one of ordinary skill in the art to provide distinct populations of fetal porcine spinal cord cells for use in xenogeneic transplantation into damaged spinal cord areas.

For the reasons of record and the reasons set forth above, the rejections are maintained.

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet M. Kerr whose telephone number is (703) 305-4055. Should the examiner be unavailable, inquiries should be directed to Deborah Clark, Supervisory Primary Examiner of Art Unit 1633, at (703) 305-4051. Any administrative or procedural questions should be directed to Kimberly Davis, Patent Analyst, at (703) 305-3015. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 305-7401.

Janet M. Kerr, Ph.D.
Patent Examiner
Group 1600

DEBORAH J. R. CLARK
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600